

09/979,509

(FILE 'HOME' ENTERED AT 07:37:00 ON 11 APR 2003)

FILE 'REGISTRY' ENTERED AT 07:37:06 ON 11 APR 2003

L1 STRUCTURE UPLOADED
L2 0 S L1
L3 157 S L1 FUL

FILE 'CAPLUS, USPATFULL' ENTERED AT 07:38:28 ON 11 APR 2003

L4 58 S L3
L5 59727 S (MAG OR MYELIN ASSOC? GLYCOPROTEIN) (3A) (PROMOT? OR EXPRESS?)
L6 1 S L4 AND L5

=> dup rem l4
PROCESSING COMPLETED FOR L4
L7 58 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l4 1-58 bib,abs

L4 ANSWER 1 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 2001:868218 CAPLUS
DN 136:694
TI Thromboxane inhibitors, compositions, and methods for therapeutic use
IN Saenz de Tejada, Inigo
PA Nitromed, Inc., USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001089519	A1	20011129	WO 2001-US16318	20010522
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	US 2003050305	A1	20030313	US 2002-285620	20021101
PRAI	US 2000-205536P	P	20000522		
	WO 2001-US16318	A1	20010522		

OS MARPAT 136:694

AB The invention describes methods for treating or preventing sexual dysfunctions in males and females, and for enhancing sexual responses in males and females, by administering a therapeutically effective amt. of at least one thromboxane inhibitor, and, optionally, at least one compd. that donates, transfers, or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase, and/or at least one vasoactive agent. The male or female may preferably be diabetic. The invention also provides compns. comprising at least one thromboxane inhibitor, and, at least one compd. that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase, and, optionally, at least one therapeutic agent, such as, vasoactive agents, nonsteroidal antiinflammatory compd.

(NSAIDs), selective cyclooxygenase-2 (COX-2) inhibitors, anticoagulants, angiotensin converting enzymes (ACE) inhibitors, angiotensin II receptor antagonists, renin inhibitors, and mixts. thereof. The invention further provides methods for treating or preventing ischemic heart disorders, myocardial infarction, angina pectoris, stroke, migraine, cerebral hemorrhage, cardiac fatalities, transient ischemic attacks, complications following organ transplants, coronary artery bypasses, angioplasty, endarterectomy, atherosclerosis, pulmonary embolism, bronchial asthma, bronchitis, pneumonia, circulatory shock of various organs, nephritis, graft rejection, cancerous metastases, pregnancy-induced hypertension, preeclampsia, eclampsia, thrombotic and thromboembolic disorders, intrauterine growth, gastrointestinal disorders, renal diseases and disorders, disorders resulting from elevated uric acid levels, and dysmenorrhea, and for inhibiting platelet aggregation or platelet adhesion or relaxing smooth muscles. The compds. and/or compns. of the present invention can also be provided in the form of a pharmaceutical kit.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 2000:907033 CAPLUS

DN 134:51387

TI Synergistic anti-inflammatory, antiallergy, and antiasthmatic agents for treatment of arachidonate metabolism disorders

IN Kawahara, Yoshikazu; Ohmori, Hiromasa

PA Nikken Chemicals Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 7 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2000355551	A2	20001226	JP 1999-168017	19990615
PRAI	JP 1999-168017		19990615		
AB	The agents contain leukotriene-synthesizing enzyme inhibitors and thromboxane-synthesizing enzyme inhibitors. Concomitant administration of ZD-2138 and isbogrel to guinea pigs sensitized with egg white albumin resulted in 49.5% inhibition of airway contraction, vs. 6.8% and 18.3%, for ZD-2138 and isbogrel alone, resp.				

L4 ANSWER 3 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 2000:841978 CAPLUS

DN 134:13340

TI Myelin-associated glycoprotein (MAG) expression promoters

IN Kawasaki, Masakazu; Gotoh, Nobuharu; Hayashi, Yoshiharu; Kawasaki, Kazuyuki

PA Welfide Corporation, Japan

SO PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DT Patent

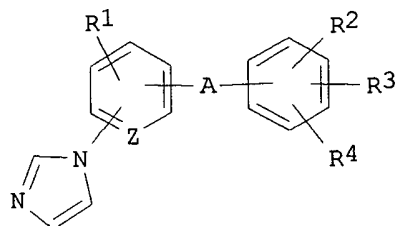
LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000071119	A1	20001130	WO 2000-JP3373	20000525
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE,				

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SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1186296 A1 20020313 EP 2000-931568 20000525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO
BR 2000011551 A 20020402 BR 2000-11551 20000525
NO 2001005733 A 20020111 NO 2001-5733 20011123
PRAI JP 1999-144336 A 19990525
WO 2000-JP3373 W 20000525
OS MARPAT 134:13340
GI



I

AB Disclosed is myelin-assocd. glycoprotein (MAG) expression promoters contg. compds. I [R1 = H, halogen, alkyl, alkoxy; R2, R3 = H, alkyl; R4 = alkyl, COOH, COOR5, CONR6R7, CH2NR6R7, CH2OH, CH2OR8 (R5, R8 = alkyl; R6, R7 = H, alkyl, imidazole); A = CH(OH); CO, CH2; Z = CH, N], optically active isomers thereof or their pharmaceutically acceptable salts. As an example of the compds. represented by the general formula I, 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid may be cited. These MAG expression promoters are useful as preventives and/or remedies for diseases of mammals including humans mainly presenting myelin hypoplasia and, in its turn, myelin sheath hypoplasia or myelin sheath destruction. A compd. Y-128 promoted axon myelination and MAG expression in Schwann cell/dorsal root ganglia (DRG) cell cocultures.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1998:527320 CAPLUS

DN 129:148981

TI Process for producing optically active imidazole derivatives and intermediates therefor

IN Kawasaki, Kazuyuki; Kobayashi, Haruhito; Ehara, Syuji; Sato, Hideaki

PA Yoshitomi Pharmaceutical Industries, Ltd., Japan

SO PCT Int. Appl., 34 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9832740	A1	19980730	WO 1998-JP150	19980114
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				

DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, KE, KG, KR,
 KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
 US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
 FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
 GA, GN, ML, MR, NE, SN, TD, TG

JP 2000290259 A2 20001017 JP 1997-10114 19970123
 AU 9854966 A1 19980818 AU 1998-54966 19980114
 EP 972768 A1 20000119 EP 1998-900397 19980114

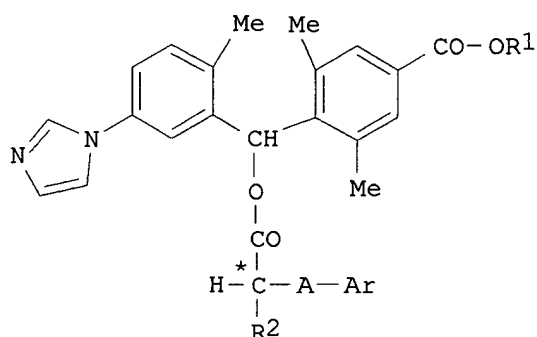
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO

US 6066739 A 20000523 US 1999-355096 19990723
 US 6166221 A 20001226 US 2000-511782 20000223

PRAI JP 1997-10114 A 19970123
 WO 1998-JP150 W 19980114

OS CASREACT 129:148981; MARPAT 129:148981

GI



AB A process for producing optically active 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid or pharmacol. acceptable salts thereof comprises optically resolving compds. represented by general formula I [R1 = alkyl, etc.; R2 = alkyl, phenylalkyl; Ar = (un)substituted Ph, etc.; A = bond, NHSO2; * indicates the (S) or (R) configuration] by fractional crystn. to give the optically active isomer thereof and then hydrolyzing the isomer. This process can provide a resoln. method useful for industrially mass-producing the optically active isomer of 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid which is useful as a thromboxane synthesis inhibitor and a preventive/remedy for diabetic complications.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1997:543473 CAPLUS

DN 127:140555

TI Preventives and remedies for complications of diabetes

IN Hayashi, Yoshiharu; Goto, Nobuharu

PA Yoshitomi Pharmaceutical Industries, Ltd., Japan; Hayashi, Yoshiharu;
 Goto, Nobuharu

SO PCT Int. Appl., 29 pp.

CODEN: PIXXD2

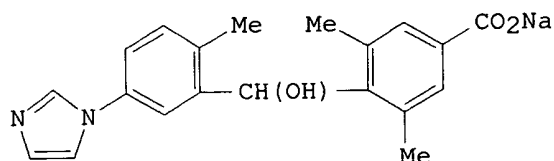
09/979,509

DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9724333	A1	19970710	WO 1996-JP3776	19961224
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2241856	AA	19970710	CA 1996-2241856	19961224
	AU 9711735	A1	19970728	AU 1997-11735	19961224
	AU 716332	B2	20000224		
	EP 881218	A1	19981202	EP 1996-942640	19961224
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CN 1209122	A	19990224	CN 1996-180052	19961224
	CN 1092645	B	20021016		
	BR 9612316	A	19990713	BR 1996-12316	19961224
	NZ 324454	A	20000929	NZ 1996-324454	19961224
	RU 2173148	C2	20010910	RU 1998-113956	19961224
	EE 3524	B1	20011015	EE 1998-208	19961224
	NO 9802988	A	19980826	NO 1998-2988	19980626
	US 6060496	A	20000509	US 1998-91993	19980626
	US 6258834	B1	20010710	US 2000-498481	20000204
	CN 1324618	A	20011205	CN 2001-117254	20010426
	US 2001036957	A1	20011101	US 2001-850000	20010508
	US 2002169194	A1	20021114	US 2002-80660	20020225
PRAI	JP 1995-340161	A	19951227		
	WO 1996-JP3776	W	19961224		
	US 1998-91993	A3	19980626		
	US 2000-498481	A3	20000204		
	US 2001-850000	B1	20010508		
AB	This document discloses (a) preventives and remedies for complications of diabetes contg. as the active ingredient 4-[(.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, optical isomers thereof or pharmaceutically acceptable salts thereof; (b) and a method for preventing or treating complications of diabetes by administering the above compds. in an efficacious dose. These drugs are useful in the prevention and treatment of complications of diabetes such as diabetic neuropathy, nephropathy, ocular disorders and arterial sclerosis. Moreover, they can exhibit long lasting effects even in an extremely small dose, which makes it possible to take the drugs only once a day. The bioactivity of 4-[(.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid in a variety of diabetes models is given in this document: this compd. showed potent therapeutic effect at 1 mg/kg in rats. Formulations contg. compds. of this invention are given.				
L4	ANSWER 6 OF 58 CAPLUS COPYRIGHT 2003 ACS				
AN	1994:314966 CAPLUS				
DN	120:314966				
TI	Y-20811: a long-acting thromboxane A2 synthase inhibitor				
AU	Matsumoto, Yasuhiro; Mikashima, Hiroshi				
CS	Tokyo Res. Lab., Yoshitomi Pharm. Ind., Saitama, Japan				
SO	Cardiovascular Drug Reviews (1993), 11(3), 283-98				
	CODEN: CDREEA; ISSN: 0897-5957				

09/979,509

DT Journal; General Review
LA English
GI



AB A review with 53 refs. Chem. and pharmacol. of the long-acting thromboxane A2 synthase inhibitor, Y-20811 (I), are discussed.

L4 ANSWER 7 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1994:182679 CAPLUS

DN 120:182679

TI Effect of Y-20811, a thromboxane A2 synthetase inhibitor, on the arachidonic acid-induced response in the blood-superfused canine coronary artery

AU Matsumoto, Yasuhiro; Noguchi, Yutaka; Inui, Jun

CS Tokyo Res. Lab., Yoshitomi Pharm. Ind., Ltd., Iruma, 358, Japan

SO Nippon Yakurigaku Zasshi (1994), 103(2), 59-66

CODEN: NYKZAU; ISSN: 0015-5691

DT Journal

LA Japanese

AB Effects of Y-20811, a thromboxane A2 synthetase inhibitor, on the arachidonic acid (AA)-induced responses were investigated in the isolated canine coronary artery superfused with blood from a donor dog and Krebs-Henseleit soln. When the coronary artery was superfused with Krebs-Henseleit soln., AA did not have any remarkable effect on its tone. In the coronary artery superfused with blood, AA (10-100 .mu.g) caused phasic constriction followed by relaxation. After denudation of the endothelium, the contractile response was augmented, and the relaxant effect was abolished. Y-20811 (1 mg/kg, i.v.), administered to the donor dog, inhibited the contraction and augmented the relaxation. Indomethacin (5 mg/kg, i.v.) and aspirin (30 mg/kg, i.v.) also inhibited the AA-induced contraction. Indomethacin inhibited the relaxation induced by AA (10-100 .mu.g), whereas aspirin inhibited the relaxation induced by a low dose of AA (10-30 .mu.g). These results suggest that Y-20811 inhibits the TXA2-induced contraction and augments the prodn. of the relaxant metabolite of AA in the coronary artery.

L4 ANSWER 8 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1993:485685 CAPLUS

DN 119:85685

TI Effect of Y-20811, a thromboxane synthetase inhibitor, on photochemically induced cerebral embolism in rabbits

AU Fujimura, M.; Mikashima, H.

CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Yoshitomi, 871, Japan

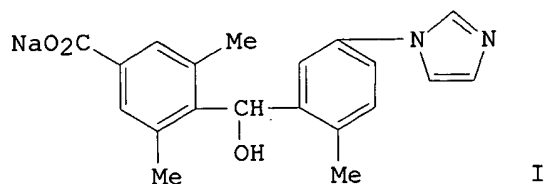
SO Thrombosis Research (1993), 70(3), 233-44

CODEN: THBRAA; ISSN: 0049-3848

DT Journal

LA English

GI



AB The effect of Y-20811 (I), a selective thromboxane A2 synthetase inhibitor, was investigated on cerebral embolism using a new model of embolic cerebral infarction in rabbits. Most of cerebral infarctions were obsd. in the hemisphere, ipsilateral to the irradiated carotid artery. Cerebral infarction, ranging from 0.2 to 1.0 mm in size, appeared only on the surface of the cortex. The platelet emboli were identified in the carotid artery and cortex arteriole by light microscopy. In this study, 83% of the control group had cerebral infarction. Y-20811 significantly suppressed the infarction no. and the incidence at doses of 1 mg/kg and 10 mg/kg (p.o.), resp. Aspirin significantly inhibited the infarction no. at a dose of 10 mg/kg, but its inhibitory effect decreased at 30 mg/kg. Ticlopidine showed no effect even at a dose of 300 mg/kg. These results indicate that Y-20811 may be useful in preventing embolic cerebral infarction and transient ischemic attacks.

L4 ANSWER 9 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1993:225217 CAPLUS

DN 118:225217

TI Effect of the combination of anticoagulant and thromboxane synthetase inhibitor (Y-20811) or receptor blockade (S-1452) on preventing thrombotic cyclic coronary flow reduction in dogs with coronary stenosis

AU Fujii, Takashi; Matsuzaki, Masunori; Oda, Tsuyoshi; Sakai, Hisanori; Tanaka, Nobuaki; Yano, Masafumi; Miura, Toshiro; Kohno, Michihiro; Katayama, Kazuhiro; Kusakawa, Reizo

CS Sch. Med., Yamaguchi Univ., Ube, Japan

SO Japanese Circulation Journal (1992), 56(11), 1191-7

CODEN: JCIRA2; ISSN: 0047-1828

DT Journal

LA English

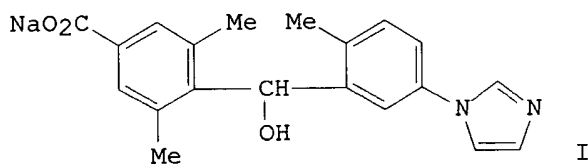
AB We examd. the hypothesis that combined actions of anticoagulant (heparin) and Y-20811, thromboxane A2 synthetase inhibitor (TXSI), or S-1452, receptor blockade (TXRB), can provide better antithrombotic protection than TXSI or TXRB alone. In 20 of 33 dogs instrumented, placement of a crit. stenosis at a focus of coronary vascular injury initiated a reproducible cyclic coronary flow redn. (CCFR). TXSI (1 mg/kg, IV) perfectly inhibited CCFR in 6 of 10 dogs (60%), and was assocd. with a significant decrease in 11-dehydro-TXB2 (85% of control) and an increase in 6-keto-PGF1.alpha. (155%) in coronary sinus blood samples. In the remaining 4 dogs, addnl. administration of heparin (2000 IU) completely abolished CCFR. On the other hand, TXRB (1 mg/kg, IV) perfectly inhibited CCFR in 7 of 10 dogs (70%), and was accompanied by a significant increase in 6-keto-PGF1.alpha. (214%) and unchanged TXB2 level. In the remaining 3 dogs, addnl. administration of heparin (2000 IU) completely abolished CCFR. Thus, the combination of anticoagulant and TXSI or TXRB were more effective than TXSI or TXRB alone in abolishing thrombotic CCFR, suggesting that the combination might be effective for treating patients with impending myocardial infarction.

L4 ANSWER 10 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1993:183119 CAPLUS

DN 118:183119

- TI Effects of a thromboxane synthetase inhibitor, Y-20811, on infarct size, neutrophil accumulation, and arrhythmias after coronary artery occlusion and reperfusion in dogs
- AU Sato, Naoki; Endo, Takao; Kiuchi, Kaname; Hayakawa, Hirokazu
- CS 1st Dep. Intern. Med., Nippon Med. Sch., Tokyo, 113, Japan
- SO Journal of Cardiovascular Pharmacology (1993), 21(3), 353-61
CODEN: JCPCDT; ISSN: 0160-2446
- DT Journal
- LA English
- AB To examine effects of a new thromboxane synthetase inhibitor, Y-20811, on infarct size, neutrophil accumulation, and arrhythmias, coronary artery was occluded for 90 min and reperfused for 6 h in anesthetized dogs. Y-20811 administered i.v. 30 min before occlusion decreased serum thromboxane B₂ (TBX₂) formation by 98% 30 min later and by 79% at 6 h after reperfusion. Ventricular fibrillation (VF) developed in 1 of 15 control and 3 of 10 treated dogs during occlusion ($p = \text{NS}$), whereas after reperfusion it occurred in 7 of 14 control and none of seven treated dogs. The no. of arrhythmias during the first hour of reperfusion was significantly reduced in treated dogs (134 beats/min in control vs. 14 beats/min in treated dogs). Hemodynamics, area at risk, and collateral flow to the ischemic region were similar for the two groups. The extent of myocardial necrosis was 28.0% of the area at risk in control dogs and 27.6% in treated dogs. The relation between the ratio of myocardial necrosis to area at risk and collateral flow was similar. The degree of neutrophil accumulation did not differ but correlated with infarct size. Thus, Y-20811 reduced reperfusion arrhythmias but failed to limit infarct size and neutrophil accumulation after coronary artery occlusion/reperfusion in dogs.
- L4 ANSWER 11 OF 58 CAPLUS COPYRIGHT 2003 ACS
- AN 1993:32705 CAPLUS
- DN 118:32705
- TI Effects of antithrombotic drug, Y-20811 on mural thrombus formation and intimal thickening following intimal injury
- AU Hayashi, Tohru; Asada, Yujiro; Kisanuki, Atsushi; Sumiyoshi, Akinobu
- CS 1st Dep. Pathol., Miyazaki Med. Coll., Miyazaki, 889-16, Japan
- SO Thrombosis Research (1992), 67(1), 81-94
CODEN: THBRAA; ISSN: 0049-3848
- DT Journal
- LA English
- GI



- AB Inhibitory effect of Y-20811 (I) on platelet thrombus formation induced by mech. intimal injury and subsequent intimal fibrous thickening was studied. In the short term expt., polyethylene tubing was inserted into the rabbit aorta and was drawn out one hour after with or without Y-20811 administration, then the rabbits were sacrificed. In the expt. for the quant. anal. of platelet adhesion, ⁵¹Cr-labeled platelets were used. Radioactivities of 2-cm length of the injured segment of the thoracic aorta and the proximal 2cm of the normal segment were measured.

Radioactivity of the injured segment was significantly lower in rabbits treated with Y-20811 than the control ones. The mean thickness (area of thrombi/length of injured intima) and the maximal thickness of the mural thrombi in the Y-20811-treated rabbits were significantly lower than those in control rabbits. De-endothelialized areas showed raised platelet thrombi in the control group and diffuse thin-layered platelet sheets in Y-20811-treated rabbits. In the long-term expt., polyethylene tubing was in-dwelling for 24 h. Rabbits were sacrificed 10 days after drawing out the tubing. Through the expt. Y-20811 was injected i.v. every 24 h. There was no significant difference between the control group and the Y-20811-treated one in both mean thickness and maximal thickness of the intimal fibromuscular thickening. The expts. indicate that Y-20811 has an inhibitory effect on platelet thrombus formation following the intimal injury, but subsequent myointimal thickening is not inhibited by the drug.

L4 ANSWER 12 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1993:20295 CAPLUS

DN 118:20295

TI Photochemically induced thrombosis of the rat coronary artery and functional evaluation of thrombus formation by occurrence of ventricular arrhythmias. Effects of acetylsalicylic acid and a thromboxane A2 synthetase inhibitor of thrombus formation

AU Fukuchi, Miho; Uematsu, Toshihiko; Araki, Seiichi; Nakashima, Mitsuyoshi
CS Sch. Med., Hamamatsu Univ., Hamamatsu, 431-31, Japan

SO Naunyn-Schmiedeberg's Archives of Pharmacology (1992), 346(5), 550-4
CODEN: NSAPCC; ISSN: 0028-1298

DT Journal

LA English

AB During i.v. infusion of rose bengal (48 mg/kg/h), the proximal portion of the rat left coronary artery was illuminated from the outside of the myocardium by green light (540 nm) to produce a transluminal thrombus subsequent to endothelial damage. The primary endothelial damage within the illuminated vascular portion, which resulted from the photochem. reaction between the dye and green light, and the subsequent formation of transluminal blood platelet-rich thrombus, were easily revealed by both light and electron microscopy. The thrombus formation was accompanied by the occurrence of heart ventricular arrhythmias due to myocardial ischemia. The times required to initiate ventricular premature beats (VPBs) and ventricular tachycardia (VT) were 381 and 444 s, resp. Pretreatment of rats with acetylsalicylic acid (3 and 10 mg/kg i.v.) before the initiation of illumination had no effect on the times required to exhibit the first VPBs and VT; the incidences of both types of arrhythmias were not reduced and the thrombus was finally formed. Pretreatment with Y-20811, a TXA2 synthetase inhibitor (0.3, 1, and 3 mg/kg i.v.), delayed the onset of both VPB and VT in a dose-dependent manner. The incidences of VPBs and VT were reduced at 1 and 3 mg/kg, and the thrombus formation was prevented. The formation of a transluminal thrombus in the left coronary artery by the present technique was highly reproducible and could be functionally evaluated by the occurrence of ventricular arrhythmias.

L4 ANSWER 13 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1992:584601 CAPLUS

DN 117:184601

TI Arterial thrombosis model with photochemical reaction in guinea pig and its property

AU Takiguchi, Y.; Hirata, Y.; Wada, K.; Nakashima, M.

CS Sch. Med., Hamamatsu Univ., Hamamatsu, 431-31, Japan

SO Thrombosis Research (1992), 67(4), 435-45

CODEN: THBRAA; ISSN: 0049-3848

DT Journal
LA English

AB The authors have already developed an arterial thrombosis model in the rat femoral artery which utilizes a photochem. reaction between systemically injected rose bengal and transillumination with 540 nm green light from the outside of the vessel. The present study applied this model to guinea-pigs in order to produce a more suitable thrombus model for evaluation of antithrombotic drugs which act on the prostaglandin cascade. In the guinea-pig, the irradiated femoral artery was completely occluded 7 min after the injection of rose bengal (10 mg/kg) in a similar manner as in rats. The processes of primary endothelial injury and the subsequent formation of thrombi during this manipulation were obsd. by the electron microscopy. Pretreatment with aspirin and Y-20811, a thromboxane synthetase inhibitor, significantly prolonged the time required for occlusion in guinea-pigs, while these drugs were ineffective in the rats. The antithrombotic effect of vapiprost, a thromboxane A2 receptor antagonist, was more pronounced in the guinea-pigs than the rats. In conclusion, this model in guinea-pigs is more suitable for evaluating antithrombotic drugs, particularly, the action of which is exerted involving the prostaglandin cascade.

L4 ANSWER 14 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1992:400587 CAPLUS

DN 117:587

TI Effects of Y-20811, a thromboxane A2 synthetase inhibitor, on experimentally induced coronary thrombosis in anesthetized dogs

AU Matsumoto, Yasuhiro; Ochi, Hiroshi; Aihara, Kenichi; Inui, Jun; Ikegami, Kiyoteru

CS Yoshitomi Pharm. Ind., Ltd., Iruma, 358, Japan

SO European Journal of Pharmacology (1992), 213(2), 167-70

CODEN: EJPHAZ; ISSN: 0014-2999

DT Journal

LA English

AB The effects of Y-20811, a selective inhibitor of thromboxane A2 (TXA2) synthetase, on blood flow and local levels of immunoreactive thromboxane B2 (i-TXB2) and 6-keto prostaglandin F1.alpha. (i-6-keto PGF1A) in the coronary artery were investigated in the canine model of coronary thrombosis. Thrombosis was induced by applying an elec. current to the intraluminal surface of the coronary artery. The plasma levels of i-TXB2 and i-6-keto PGF1.alpha. were measured distal to the electrode. In the control group, coronary blood flow decreased and finally stopped 207 min after the start of current application. The level of i-TXB2 rose before the coronary occlusion. Coronary blood flow did not change in the Y-20811-treated group (1 mg/kg i.v.). The level of i-TXB2 decreased and remained lower than that in the control group. The level of i-6-keto PGF1.alpha. tended to increase slightly in the Y-20811-treated, but not in the control group. The wt. of the thrombus in the Y-20811-treated group was less than that in the control group. These results suggest that Y-20811 prevents coronary thrombosis by the inhibition of TXA2 prodn. around the elec. injured lumen of the coronary artery.

L4 ANSWER 15 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1992:166056 CAPLUS

DN 116:166056

TI Effect of Y-20811, a long-lasting thromboxane A2 synthetase inhibitor, on antigen-induced airway hyperresponsiveness in guinea pigs

AU Kagoshima, Masahiko; Tomomatsu, Noriko; Aratani, Hidekazu; Terasawa, Michio

CS Res. Lab., Yoshitomi Pharm. Ind., Fukuoka, 871, Japan

SO International Archives of Allergy and Applied Immunology (1991), 96(3),

09/979,509

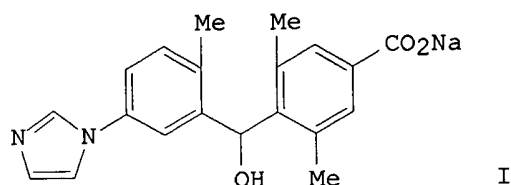
238-43

CODEN: IAAAAAM; ISSN: 0020-5915

DT Journal

LA English

GI



AB The effect of Y-20811 (I) on airway hyperresponsiveness was studied in sensitized guinea pigs. Airway hyperresponsiveness to acetylcholine (ACh) reached max. 7 h after antigen challenge in guinea pigs sensitized actively. I (0.3-3 mg/kg) administered orally 3 h prior to challenge inhibited this airway hyperresponsiveness in a dose-dependent manner. I (3 mg/kg) administered orally 4 h after antigen challenge also decreased the airway hyperresponsiveness. On the other hand, I did not affect the bronchoconstriction induced by ACh, serotonin and histamine in nonsensitized guinea pigs. The no. of eosinophils in bronchoalveolar lavage fluid in the guinea pig reached the peak 7 h after antigen challenge. I had a tendency to decrease the no. of total cells, macrophages and eosinophils in a dose-dependent manner. I suppress the asthmatic mechanism which causes antigen-induced airway hyperresponsiveness.

L4 ANSWER 16 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1992:143580 CAPLUS

DN 116:143580

TI Irreversible inhibition of thromboxane (TX) A2 synthesis by Y-20811, a selective TX synthetase inhibitor

AU Mikashima, Hiroshi; Ochi, Hiroshi; Muramoto, Yoshito; Hirotsu, Kyouichi; Arima, Noriyuki

CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Fukuoka, 871, Japan

SO Biochemical Pharmacology (1992), 43(2), 295-9

CODEN: BCPA6; ISSN: 0006-2952

DT Journal

LA English

AB Since Y-20811 has been reported to inhibit serum thromboxane (TX) A2 prodn. with a long duration of action, its mechanism of action was investigated. When [3H]Y-20811 (3 mg/kg) was administered orally to rats, the peak platelet concn. of Y-20811 was obtained 1 h after the administration, and the T1/2 was 43 h. The peak plasma concn. of Y-20811 was also obtained 1 h after administration, but the elimination of Y-20811 from plasma was faster (T1/2.alpha. = 1.5 h, T1/2.beta. = 15 h) than that obsd. in platelets. Serum TXA2 (estd. as TXB2) prodn. was inhibited from 1 to 72 h after the oral administration of unlabeled Y-20811 (3 mg/kg), which temporally resembled the change of the platelet Y-20811 concn. In platelet-rich plasma, [3H]Y-20811 completely inhibited TXA2 prodn. at about 1500 pg/109 platelets, and the IC50 level was about 600 pg/109 platelets, which was similar to values obtained in ex vivo studies. In addn., inhibition of TXA2 prodn. by Y-20811 still remained after washing the drug-pretreated microsomes, whereas that of dazoxiben completely disappeared. A similar irreversible inhibition of TXA2 prodn. was obsd.

with aspirin. These results suggest that Y-20811 may firmly combine with platelet TX synthetase and may irreversibly inhibit TXA2 prodn.

L4 ANSWER 17 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1991:407736 CAPLUS

DN 115:7736

TI Chromatographic separation of optically-active isomers

IN Sakai, Junichi; Ikeda, Kuniki; Hamazaki, Toshio; Kono, Hisashi; Ogawa, Takayuki; Matsumoto, Takashi

PA Yoshitomi Pharmaceutical Industries, Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 03027326	A2	19910205	JP 1989-134256	19890526
	JP 07080793	B4	19950830		
PRAI	JP 1989-134256		19890526		

AB Optically-active isomers are chromatog. sepd. using polysaccharide substituted-arom. carbamate deriv. as a chiral stationary phase and a mixt. of H2O-sol. org. solvents and H2O or buffers contg. various salts as a mobile phase. Na (.+-.)-4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-2,5-dimethylbenzoate dihydrate was charged on a column packed with cellulose tris(3,5-dimethylphenyl)carbamate and eluted with a mixt. of a NaClO4-HClO4 buffer and MeCN, vol. ratio, sepn. factor, and sepn. rate were 4.64, 1.57, and 2.68, resp.

L4 ANSWER 18 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1991:400544 CAPLUS

DN 115:544

TI Effects of Y-20811, a specific thromboxane A2 synthetase inhibitor, on chemical mediator-induced bronchoconstriction in guinea pigs

AU Kagoshima, Masahiko; Tomomatsu, Noriko; Fukuda, Tetsuko; Mikashima, Hiroshi; Terasawa, Michio

CS Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan

SO Nippon Yakurigaku Zasshi (1991), 97(5), 277-86

CODEN: NYKZAU; ISSN: 0015-5691

DT Journal

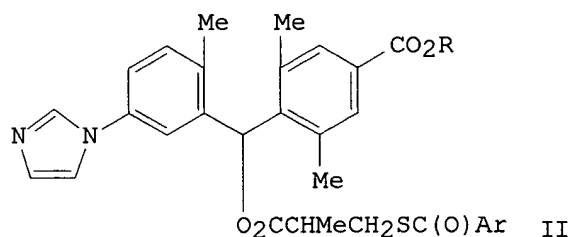
LA Japanese

AB The effects of Y-20811 on chem. mediator-induced bronchoconstriction and the release of chem. mediators into lung perfusion fluid during arachidonic acid (AA)-induced bronchoconstriction were examd. in guinea pigs. Y-20811 (0.01-1 mg/kg, i.v.), like acetylsalicylic acid or indomethacin, dose-dependently suppressed arachidonic acid- and LTD4-induced bronchoconstriction, and it (1 mg/kg, i.v.) also inhibited PAF-induced bronchoconstriction in guinea pigs. However, at a dose of 1 mg/kg, i.v., it was inactive against the bronchoconstriction induced by histamine, serotonin, and acetylcholine in guinea pigs. Y-20811 (0.3-10 mg/kg) administered orally also prevented the LTD4-induced bronchoconstriction in a dose-dependent manner. This protective effect of Y-20811 (10 mg/kg, p.o.) persisted for at least 24 h. Y-20811 (10 mg/kg, p.o.) also inhibited antigen-induced bronchoconstriction in guinea pigs passively sensitized with anti-ovalbumin guinea pig serum and pretreated with mepyramine. In the perfused and ventilated guinea pig lungs, Y-20811 inhibited AA-induced bronchoconstriction, decreased the release of TXA2 (estd. as TXB2), and increased the release of PGE2 into the perfused lung fluid, significantly (TXB2 and PGE2 were measured by HPLC). Therefore, Y-20811 suppressed various stimulant-induced bronchoconstrictions through

the decrease of TXA2 prodn. and the increase of PGE2 prodn. Thus, Y-20811 should prove useful as an antiasthmatic drug.

L4 ANSWER 19 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1991:101990 CAPLUS
 DN 114:101990
 TI Preparation of optically active 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid by separation of diastereoisomeric esters
 IN Tsuruta, Mineo; Oe, Takanori; Shiotsuki, Yoshiko; Matsumoto, Takashi; Yokobe, Tetsuro
 PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 7 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 02215771	A2	19900828	JP 1989-35684	19890214
PRAI	JP 1989-35684		19890214		
OS	MARPAT 114:101990				
GI					

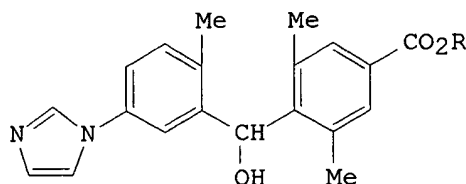


AB Racemic title compd. (I), known thromboxane synthase inhibitor useful for treatment of thrombosis, asthma, and nephritis (no data), is resolved by sepn. of its diastereoisomeric esters [II; R = lower alkyl, (substituted) phenylalkyl; Ar = (substituted) Ph, naphthyl, thienyl, furyl, or pyridyl; C* having (S)-(-) or (R)-(+) configuration] on a column chromatog. followed by hydrolysis. Thus, benzylation of (.+.)-4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid Na salt with 2-ClC₆H₄CH₂Cl in DMF at 45-50.degree. and esterification of the resulting 2-chlorobenzyl ester with (S)-(-)-2-methyl-3-(3,5-dinitrobenzoylthio)propionyl chloride in pyridine/CH₂CH₂ gave (S)-(-)-I [R = CH₂C₆H₄Cl-2, Ar = C₆H₃(NO₂)₂-3,5] which (67 g) was subjected to a silica gel chromatog. eluting with a 200:3:3 mixt. of EtOAc-MeOH-H₂O to give 26 g (+)-diastereoisomeric ester and 24.1 g (-)-diastereoisomeric ester which were deacylated with EtONa in EtOH to give (-)-I and (+)-I, resp.

L4 ANSWER 20 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1990:637668 CAPLUS
 DN 113:237668
 TI Effect of additives on the dissolution of Y-20811, a new thromboxane synthetase inhibitor
 AU Shiotsuki, Takako; Kino, Shigemi; Ogawa, Kenji; Yokobe, Tetsuo
 CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
 SO Yakuzaigaku (1990), 50(2), 107-12
 CODEN: YAKUA2; ISSN: 0372-7629

09/979,509

DT Journal
LA English
GI



I, R=Na
II, R=H @ H₂SO₄

AB Compressed tablets of Y-20811 (I) and sulfate salt (II) were prepd. and their dissoln. behaviors from tablets compared. The dissoln. rate of active ingredients from tablets contg. I was significantly higher than those contg. II. A great increase in the dissoln. rate was obsd. when tablets of I were prepd. with NaHCO₃, D-mannitol and a water-sol. polymer such as polyvinylpyrrolidone K-30 (PVP K-30) or hydroxypropyl cellulose-L (HPC-L). In order to improve the dissoln. rate of the drug, fine granules of I were prepd. with some additives, by referring the formulation of the above tablets. The addn. of NaHCO₃ and HPC-L to the granules facilitated significantly the drug-release in the dissoln. media over the pH range of 1.2 to 6.5. The enhancing effects of NaHCO₃ and HPC-L may be ascribable to a increase in microenvironmental pH around granules and an inhibition of the deposition of I after acid dissoln., resp.

L4 ANSWER 21 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1990:637667 CAPLUS

DN 113:237667

TI Dissolution and absorption characteristics of new thromboxane synthetase inhibitors

AU Iwata, Toshio; Akiyama, Yohichi; Shiotsuki, Takako; Iwata, Akihiro; Isobe, Masao; Takamatsu, Rikuo; Yokobe, Tetsuo

CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan

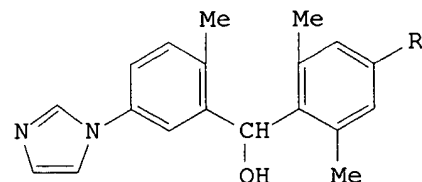
SO Yakuzaigaku (1990), 50(2), 101-6

CODEN: YAKUA2; ISSN: 0372-7629

DT Journal

LA English

GI

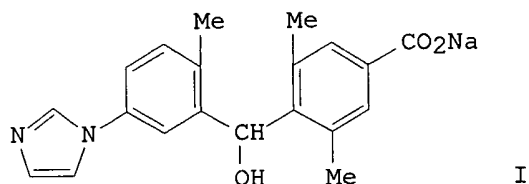


I, R=CO₂H
II, R=Me

AB The in vitro dissoln. characteristics of five new thromboxane synthetase inhibitors were evaluated by using the pH controlled dissoln. system which can mimic the physiol. pH conditions in the gastrointestinal tract. The Na salt and the sulfate of 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid (I) were dissolved rapidly in the acidic medium and remained stable in soln. even in the neutral medium,

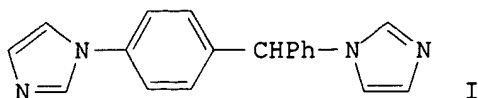
while the dissoln. of I was insufficient over the pH range tested. The deriv. (II) and its hydrochloride dissolved rather slowly in the acidic medium, and part of them gradually crystd. out of soln. with increasing pH, due to the low aq. soly. of the neutral form of II. The in vivo absorption studies using beagle dogs revealed that the two salts of I showed excellent oral bioavailability, where the shorter the mean absorption time, the greater the extent of bioavailability.

L4 ANSWER 22 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1990:618090 CAPLUS
 DN 113:218090
 TI Optimization of tablets formulation for Y-20811, a new thromboxane synthetase inhibitor
 AU Kino, Shigemi; Shiotsuki, Takako; Gotoh, Mizumi; Oda, Minoru; Ogawa, Kenji; Yokobe, Tetsuo
 CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
 SO Yakuzaigaku (1990), 50(2), 113-18
 CODEN: YAKUA2; ISSN: 0372-7629
 DT Journal
 LA Japanese
 GI



AB The formulation design of Y-20811(I) for oral dosage form was investigated. Hydroxypropyl Me cellulose 2910 was selected as a binder candidate. The exptl. design technique was applied to optimize the formulation of 50 mg tablets. Dissoln. parameters of the tablets were predicted as a function of the amts. of D-mannitol and NaHCO₃. An optimum formulation of the tablets was proposed on the basis of these predictions. The tablets thus obtained showed a significantly facilitated drug-release in the dissoln. test media over the physiol. pH conditions in the gastrointestinal tract.

L4 ANSWER 23 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1990:478279 CAPLUS
 DN 113:78279
 TI Researches on antibacterial and antifungal agents. XII. Analogs of bifonazole with two imidazole moieties and related azoles
 AU Stefancich, Giorgio; Silvestri, Romano; Panico, Salvatore; Artico, Marco; Simonetti, Nicola
 CS Dip. Studi Farm., Univ. Roma "La Sapienza", Rome, 00185, Italy
 SO Archiv der Pharmazie (Weinheim, Germany) (1990), 323(5), 273-80
 CODEN: ARPMAS; ISSN: 0365-6233
 DT Journal
 LA English
 OS CASREACT 113:78279
 GI



AB Bifonazole analogs, bearing 2 imidazole rings or related azole rings, were prepd. and tested as antifungal agents. E.g., reaction of PhCOC₆H₄F-p with imidazole/NaH, followed by NaBH₄ redn., chlorination with SOCl₂, and reaction with imidazole/Et₃N gave the diimidazole deriv. I. Also prepd. were tetrazolyl and triazolyl derivs. These analogs possessed only a fraction of the antifungal activity of bifonazole.

L4 ANSWER 24 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1990:429252 CAPLUS

DN 113:29252

TI Pharmaceutical compositions containing thromboxane synthetase inhibitor

IN Oda, Minoru; Kino, Shigemi; Ogawa, Kenji; Shiotsuki, Takako

PA Yoshitomi Pharmaceutical Industries, Ltd., Japan

SO PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO. 8906959	A1	19890810	WO 1989-JP100	19890131
	W: US				
	RW: AT, BE, CH, DE, FR, GB, IT, NL, SE				
	EP 379579	A1	19900801	EP 1989-901749	19890131
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
	JP 02000704	A2	19900105	JP 1989-24495	19890201
	US 5091191	A	19920225	US 1989-415356	19890925
PRAI	JP 1988-23250		19880203		
	WO 1989-JP100		19890131		

AB A pharmaceutical compn. comprises Na 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate (I) or its optical isomer or hydrates having improved releasability and further contains D-mannitol and/or NaHCO₃ and a water-sol. high-mol. compd. This compn. can release I irresp. of the pH in digestive tract including stomach. Thus, I 10 and D-mannitol 90% by wt. were mixed with H₂O, made into particles, and dried at 50.degree. to give a pharmaceutical powder sol. in the stomach for the treatment of thrombosis and asthma (no pharmacol. data).

L4 ANSWER 25 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1990:400316 CAPLUS

DN 113:316

TI Correlation between pharmacokinetics and pharmacologic effects of a new imidazole thromboxane synthetase inhibitor

AU Iwata, Toshio; Mikashima, Hiroshi; Takamatsu, Rikuo

CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan

SO Journal of Pharmaceutical Sciences (1990), 79(4), 295-300

CODEN: JPMSAE; ISSN: 0022-3549

DT Journal

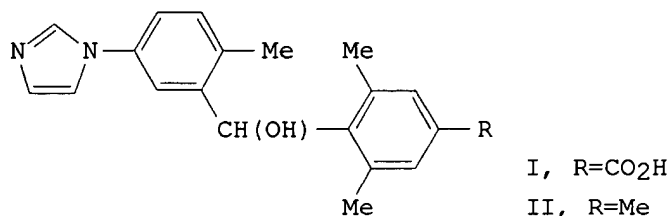
LA English

AB A new imidazole deriv., sodium 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate dihydrate (I; Y-20811), is a potent selective inhibitor of thromboxane (TX) synthetase and a candidate drug for preventing ischemic circulatory disorders. After oral dosing in

beagle dogs, I persistently inhibited TX prodn., although the elimination of the drug was relatively rapid from plasma. The amt. of drug distributed in platelets was small. However, I was eliminated from platelets very slowly ($t_{1/2} = 41-130$ h), the rate of elimination being comparable to the turnover rate of platelets. From the in vitro expts., an obvious pos. correlation was noted between the amt. of the drug bound with TX synthetase in platelets and the inhibition of TX prodn. This correlation suggested that the small amt. of I detected in platelets in vivo was large enough to inhibit TX prodn. From these observations, I is thought to dissoc. extremely slowly from the active sites of TX synthetase. Consequently, the duration of the effect was dependent on the turnover of platelets.

L4 ANSWER 26 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:191692 CAPLUS
DN 112:191692
TI Protective effect of Y-20811, a long-lasting thromboxane synthetase inhibitor, on endotoxin shock in rabbits
AU Mikashima, Hiroshi; Muramoto, Yoshito
CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Yoshitomi, 871, Japan
SO Thrombosis Research (1990), 57(4), 499-505
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English
AB The effect of sodium 4-[.alpha.-hydroxy-5-(imidazolyl)-2-methylbenzyl]-3,5-dimethyl benzoate dihydrate (Y-20811), a selective thromboxane (TX) synthetase inhibitor, on endotoxin shock was investigated in comparison with aspirin. The drugs were orally administered to rabbits at 24 and 1 h before injection of endotoxin (5 mg/kg, i.v.). Y-20811 (1 mg/kg) promoted the recovery of decreased platelet counts and inhibited hypotension induced by endotoxin. It also inhibited the increase in plasma TXB2 and 6-ketoPGF1.alpha.. Aspirin at 30 mg/kg, inhibited hypotension and the increase in both plasma TXB2 and 6-ketoPGF1.alpha. levels, but it failed to inhibit the decrease in platelet counts. In the control group, all rabbits died within 180 min after endotoxin injection, while Y-20811 completely protected animals against death at a dose of 0.3 mg/kg. Aspirin also protected animals against death at a dose of 30 mg/kg, which was, however, about one hundredth as potent as Y-20811. These results indicate that Y-20811 is useful in treating endotoxin shock.

L4 ANSWER 27 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:185659 CAPLUS
DN 112:185659
TI Physicochemical properties of new thromboxane synthetase inhibitors, Y-20811 and its related compounds
AU Shiotsuki, Takako; Ogawa, Kenji; Yokobe, Tetsuo
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
SO Yakuzai-gaku (1989), 49(3), 227-33
CODEN: YAKUA2; ISSN: 0372-7629
DT Journal
LA Japanese
GI



AB Salts of thromboxane synthetase inhibitors I and II, i.e. I Na (III) (Y-20811), I sulfate (IV), I mesylate (V), I-HCl (VI), I-L-lysine salt (VII), II sulfate (VIII), II mesylate (IX), II-HCl (X), and II fumarate (XI) were obtained as crystals. In the course of preformulation studies of I and II, physicochem. properties of their salts were evaluated. VI, VII, X and XI were unstable in stability tests. V and IX had unfavorable behavior in dissoln. tests. III, IV and VIII were free from such problems. These salts tended to form supersatd. solns. in the dissoln. test media. The mechanisms of the supersatn. of III and IV in the test media were investigated. It was proposed that their supersatn. involves accelerated dissoln. through the diffusion layers and self-buffering effects or hydrations.

L4 ANSWER 28 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1990:69359 CAPLUS

DN 112:69359

TI Pharmacokinetics of sodium 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate (Y 20811), a new thromboxane synthetase inhibitor. II. Pharmacokinetics of intact drug and main metabolite in dog

AU Iwata, Toshio; Mikashima, Hiroshi; Isobe, Masao; Takamatsu, Rikuo; Yokobe, Tetsuo

CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Fukuoka, 871, Japan

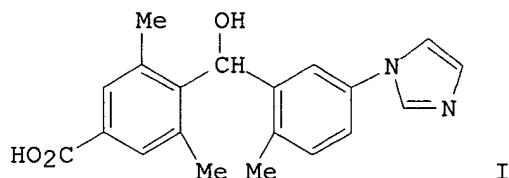
SO Yakugaku Zasshi (1989), 109(11), 853-7

CODEN: YKKZAJ; ISSN: 0031-6903

DT Journal

LA Japanese

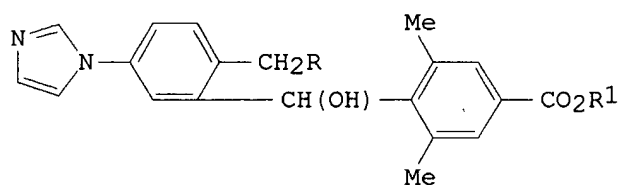
GI



AB The pharmacokinetics of Y 20811 (I-Na) in the beagle dog was investigated after oral and i.v. administration. After the administration of I-Na at 3 mg/kg (oral), 70.9% of the dose was absorbed, and the max. plasma concn. of I was obsd. at 0.33 h. After oral administration, the area under the plasma concn.-time curve of I increased almost linearly in proportion to the dose. The hydroxymethyl metabolite, II, was also detected in the plasma, but the concn. of II was lower than I. After the administration at 3 mg/kg (oral), 27.7 and 3.8% of the dose were recovered as I and II, resp., in the urine, and 32.2 and 30.1% recovered as I and II in the feces. Therefore, 93.8% of the dose was totally recovered within 5 days. The inhibitory effect of II on the aggregation of rabbit platelets was studied in vitro. This metabolite showed only one sixth activity of I-Na.

Thus, the inhibitory effect on the platelet aggregation of II is considered to be almost negligible in the beagle dog administered with I-Na.

- L4 ANSWER 29 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1990:20938 CAPLUS
 DN 112:20938
 TI Direct separation of enantiomers by reversed-phase high performance liquid chromatography on cellulose tris(3,5-dimethylphenylcarbamate)
 AU Ikeda, Kuniki; Hamasaki, Toshio; Kohno, Hisashi; Ogawa, Takayuki; Matsumoto, Takashi; Sakai, Junichi
 CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
 SO Chemistry Letters (1989), (6), 1089-90
 CODEN: CMLTAG; ISSN: 0366-7022
 DT Journal
 LA English
 AB Various types of enantiomeric drugs, e.g. Y-20811, were optically sep'd. by reversed-phase high performance liq. chromatog. using cellulose tris(3,5-dimethylphenylcarbamate) as a chiral stationary phase.
- L4 ANSWER 30 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1990:15886 CAPLUS
 DN 112:15886
 TI Pharmacokinetics of sodium 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate (Y-20811), a new thromboxane synthetase inhibitor. I. Isolation and structure elucidation of urinary metabolite in dogs.
 AU Iwata, Toshio; Tsuruda, Mineo; Demizu, Kenichi; Isobe, Masao; Takamatsu, Rikuo; Yokobe, Tetsuo
 CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Fukuoka, 871, Japan
 SO Yakugaku Zasshi (1989), 109(9), 636-41
 CODEN: YKKZAJ; ISSN: 0031-6903
 DT Journal
 LA Japanese
 GI

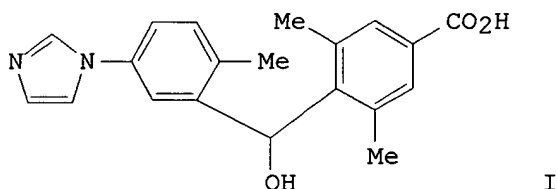


I, R=H, R¹=Na
 II, R=OH, R¹=H

- AB The urinary metabolites of Y-20811 (I) in dogs were investigated. The main metabolite was isolated by HPLC and subsequent preparative TLC. The structure of this metabolite was established as 4-[.alpha.-hydroxy-2-hydroxymethyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid (II) on the basis of spectral analyses and confirmed by its total synthesis.
- L4 ANSWER 31 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1989:614429 CAPLUS
 DN 111:214429
 TI Thromboxane synthetase inhibitors. II. Optical resolution of 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid
 AU Tsuruda, Mineo; Shiotsuki, Takako; Matsumoto, Takashi; Oe, Takanori
 CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Yoshitomi, 871, Japan

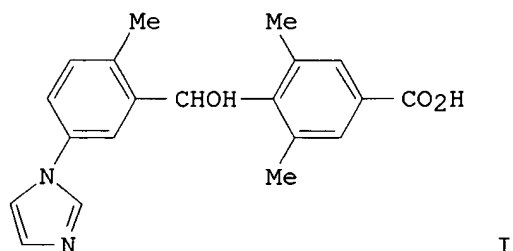
09/979,509

SO Yakugaku Zasshi (1989), 109(1), 26-32
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
OS CASREACT 111:214429
GI



AB The optical resolu. of racemic 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid (dl-I), a new potent and long lasting thromboxane synthetase inhibitor, was investigated. (S)-3-(3,5-Dinitrobenzoylthio)-2-methylpropionyl group was introduced to .alpha.-hydroxy moiety of Me ester of dl-I by three steps of reaction to give the corresponding ester compd. Then, two diastereomers of esters, were sepd. by column chromatog. using on silica gel. Alk. hydrolysis of ester enantiomers, followed by reactions with NaOEt gave optically pure sodium salts of (-)-I and (+)-I, resp. The separative detn. methods for the diastereomers of esters, and for the enantiomers of the sodium salts of dl-I by high performance liq. chromatog. were also established.

L4 ANSWER 32 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1989:534040 CAPLUS
DN 111:134040
TI Thromboxane synthetase inhibitors. I. Synthesis of some imidazolylarylmethanols and their inhibitory activity on platelet aggregation
AU Tsuruda, Mineo; Mikashima, Hiroshi; Oe, Takanori; Kawasaki, Kazuyuki; Setoguchi, Shinro; Naka, Yoichi; Tahara, Tetsuya
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Yoshitomi, 871, Japan
SO Yakugaku Zasshi (1989), 109(1), 33-45
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
OS CASREACT 111:134040
GI



AB Several imidazolylpyridinemethanols and imidazolylbenzenemethanols were

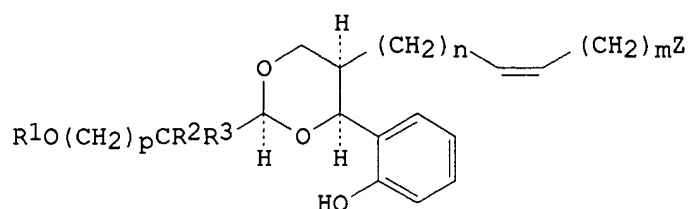
prepd. and evaluated for inhibitory activity against arachidonic acid-induced platelet aggregation. The result shows that the arylmethanol moiety is essential for the activity and may correspond to the 15-OH group of prostaglandin H₂. Among the compds. tested, imidazolylbenzyl alc. deriv. I was found to have a potent inhibitory activity and a long duration of action. Structure-activity relationships are also discussed briefly.

L4 ANSWER 33 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1989:18546 CAPLUS
 DN 110:18546
 TI Imidazole derivatives as immunostimulants
 IN Kudome, Masao; Mikashima, Hiroshi; Tsuruta, Mineo
 PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 11 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 63119425	A2	19880524	JP 1986-266455	19861107
PRAI	JP 1986-266455		19861107		
OS	MARPAT 110:18546				
GI	For diagram(s), see printed CA Issue.				
AB	The title compds. I [R ₁ = H, lower alkyl; R ₂ = H, halo, lower alkyl, alkoxy, etc.; ring A = benzene ring, pyridine ring, furan ring, thiophene ring; XY = :O, or one of X and Y is H, lower alkyl, the other is OH; Z = alkyl, cycloalkyl, aryl, heteroaryl] are tested for immunostimulating activities. In a test using mice dosed with sheep erythrocytes and cyclophosphamide, Na 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoate.2H ₂ O caused an immunorestorative response of 359% (control = 100%).				

L4 ANSWER 34 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1988:637035 CAPLUS
 DN 109:237035
 TI Therapeutic agents containing TXA₂ antagonists and TXA₂ synthesis inhibitors
 IN Smithers, Michael James
 PA Imperial Chemical Industries PLC, UK
 SO Eur. Pat. Appl., 24 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 266979	A2	19880511	EP 1987-309634	19871030
	EP 266979	A3	19891102		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	ZA 8707885	A	19880629	ZA 1987-7885	19871020
	AU 8780551	A1	19880505	AU 1987-80551	19871030
	DK 8705766	A	19880505	DK 1987-5766	19871103
	US 4925869	A	19900515	US 1987-118227	19871103
	JP 63130531	A2	19880602	JP 1987-277554	19871104
PRAI	GB 1986-26296		19861104		
OS	MARPAT 109:237035				
GI					



I

AB A TXA2 antagonist dioxane ether [I; R1 = alkyl, cycloalkyl, cycloalkylalkyl, (substituted) Ph, (substituted) phenylalkyl; R2, R3 = H, C1-4 alkyl, (alkyl-substituted) C3-6 polymethylene; Z = CO2H, 1H-tetrazol-5-yl; m = 2-4; n = 1, 2; p = 0-2] and a TXA2 formation inhibitor are useful together for treatment of disorders involving TXA2 and/or other prostanoid contractile substances. I (R1 = Ph, R2 = R3 = Me, Z = CO2H, m = 2, n = 1, p = 0) (II) was prep'd. from 4-(o-methoxyphenyl)-2,2-dimethyl-1,3-dioxan-cis-5-ylacetaldehyde by Wittig reaction with HO2CCH2CH2PPh3Br and KOtMe3 to form the 4(Z)-dioxan-5-ylhexenoic acid deriv., transketalization with 2-methyl-2-phenoxypropionaldehyde [prep'd. by redn. of PhCMe2CO2Me with (Me2CHCH2)2AlH], and removal of the methoxy Me group with Ph2PLi. An aerosol was prep'd. from a TXA2 antagonist (e.g. II) 0.1, a TXA2 synthesis inhibitor (e.g. dazoxiben or CV4151) 0.1, sorbitan trioleate 0.27, CCl3F 70.0, CCl2F2 280.0, and C2Cl2F4 1094.0 mg/mL. Human blood platelet aggregation in response to arachidonic acid was completely inhibited by a combination of II (10⁻⁹M) and dazoxiben (10⁻⁴M), whereas either agent alone was ineffective.

L4 ANSWER 35 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1988:631037 CAPLUS

DN 109:231037

TI Pharmaceutical compositions

IN Brewster, Andrew George; Brown, George Robert; Smithers, Michael James

PA Imperial Chemical Industries PLC, UK

SO Eur. Pat. Appl., 30 pp.

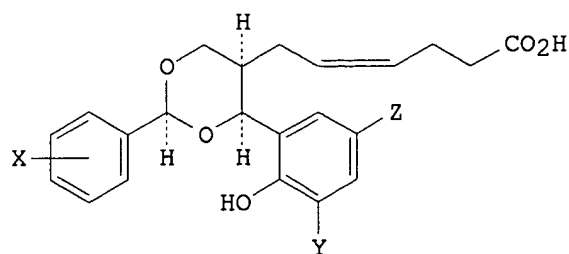
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 266980	A2	19880511	EP 1987-309635	19871030
	EP 266980	A3	19891108		
	EP 266980	B1	19921028		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	ZA 8707886	A	19880629	ZA 1987-7886	19871020
	IL 84261	A1	19911215	IL 1987-84261	19871023
	AT 81774	E	19921115	AT 1987-309635	19871030
	ES 2052581	T3	19940716	ES 1987-309635	19871030
	DK 8705768	A	19880505	DK 1987-5768	19871103
	US 4908380	A	19900313	US 1987-118226	19871103
	CA 1308660	A1	19921013	CA 1987-550880	19871103
	AU 8780698	A1	19880505	AU 1987-80698	19871104
	AU 608546	B2	19910411		
	JP 63130532	A2	19880602	JP 1987-277555	19871104
PRAI	GB 1986-26297		19861104		
	EP 1987-309635		19871030		
OS	MARPAT 109:231037				
GI					



I

AB A TXA2 antagonist 2,4-diphenyl-1,3-dioxane deriv. I (X = F, Cl, Br, F3C, cyano, MeO, O2N; 1 of Y, Z = H, F and the other = H) and a TXA2 formation inhibitor are useful together for treatment of disorders involving TXA2 and/or other prostanoid contractile substances. I (X = 2-cyano; Y = Z = H) (II) was prepd. from [4-(o-methoxyphenyl)-2,2-dimethyl-1,3-dioxan-cis-5-yl]acetaldehyde by Wittig reaction with HO2C(CH2)3PPh3Br and KOCMe3 to form the 4(Z)-dioxan-5-ylhexenoic acid deriv., followed by transketalization with o-cyanobenzaldehyde, and removal of the methoxy Me group with NaH in the presence of EtSH. Human blood platelet aggregation in response to arachidonic acid was 89.9% inhibited by a combination of I (X = 2-Cl; Y = Z = H) (10⁻⁹M) and dazoxiben (10⁻⁵M), compared to 2.2 and 4.5%, resp., for each agent used sep. A capsule was prepd. contg. a TXA2 antagonist (e.g. II) 5, a TXA2 synthetase inhibitor (e.g. dazoxiben) 5, lactose 488.5, and Mg stearate 1.5 mg.

L4 ANSWER 36 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1987:611652 CAPLUS

DN 107:211652

TI Antinephritic effect of Y-19018, a thromboxane A synthetase inhibitor, on crescentic-type anti-GBM nephritis in rats

AU Suzuki, Yoshio; Tsukushi, Yoshihito; Ito, Mikio; Nagamatsu, Tadashi

CS Fac. Pharm., Meijo Univ., Nagoya, 468, Japan

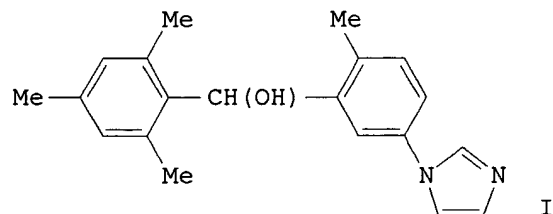
SO Japanese Journal of Pharmacology (1987), 45(2), 177-85

CODEN: JJPAAZ; ISSN: 0021-5198

DT Journal

LA English

GI



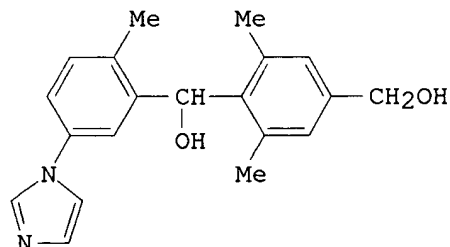
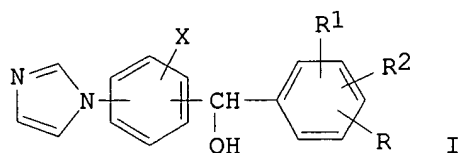
I

AB The antinephritic effect of Y-19018 (I) a thromboxane A synthetase inhibitor, on crescentic-type anti-glomerular basement membrane (anti-GBM) nephritis in rats was studied. Male Sprague Dawley rats were immunized with rabbit .gamma.-globulin in Freund's complete adjuvant following i.v.

injection of anti-GBM serum. Y-19018 at a dose of 0.3 and 3.0 mg/kg was given orally to rats from the day after the injection of anti-GBM serum (day 1) to day 39. Y-19018, 3.0 mg/kg, inhibited both urinary protein excretion (30.6%) on day 19 and plasma cholesterol (39.8%) on day 15. Moreover, light microscopy demonstrated that this drug at both doses remarkably prevented histol. involvement of the glomeruli on day 40 in a dose-dependent manner. In the blood obtained from nephritic rats, platelet aggregation was increased. Y-19018 suppressed (48.7%) the hyperaggregability of platelets on day 40 at a high dose, although the suppression of platelet aggregation was not in a dose-dependent manner. Apparently, Y-19018 shows beneficial effects on crescentic-type anti-GBM nephritis and may exert its action partly through inhibition of glomerular TXA2.

L4 ANSWER 37 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1987:515589 CAPLUS
 DN 107:115589
 TI 5-(Imidazol-1-yl)-.alpha.-(2,6-dimethylphenyl)benzenemethanol derivatives as drugs
 IN Tsuruta, Mineo; Ooe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi; Yasuda, Hiroshi
 PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 13 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62000470	A2	19870106	JP 1985-139952	19850625
	JP 05074589	B4	19931018		
PRAI	JP 1985-139952		19850625		
OS	CASREACT 107:115589				
GI					



AB The title compds. [I; R = CHO, CHR3R4 [R3 = H, alkyl; R4 = OH, alkoxy, acyloxy, (unsubstituted PhO), ZNR5R6 (Z = CO, CH2, alkylmethylene; R5, R6 = H, acyl, hydroxyalkyl, carboxyalkyl, 1-substituted piperidyl or NR5R6 = heterocyclyl); R1R2 = H, alkyl; X = H, halo, alkyl, alkoxy], useful as

inhibitors of thromboxane A2 synthesis and blood platelet aggregation (no data), were prepd. A mixt. of 5-iodo-2,2',6'-trimethyl-4'-(ethoxycarbonyl)benzophenone and imidazole contg. K2CO3, Cu powder, and KF was heated at 140.degree. for 4 h to give 5-(imidazol-1-yl)-2,2',6'-trimethyl-4'-(ethoxycarbonyl)benzophenone, which was reduced by LiAlH4 to give an .alpha.-phenylbenzyl alc. deriv. II.

L4 ANSWER 38 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1987:213946 CAPLUS

DN 106:213946

TI 4-(.alpha.-Hydroxy-3-imidazol-1-ylbenzyl)benzoates as blood platelet aggregation inhibitors

IN Tsuruta, Mineo; Oe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi; Yasuda, Hiroshi

PA Yoshitomi Pharmaceutical Industries, Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 6 pp.

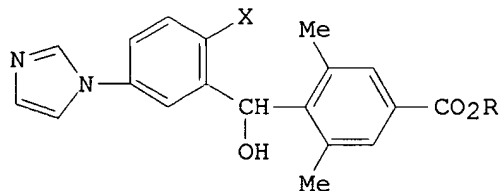
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	JP 61282366	A2	19861212	JP 1985-124617	19850607
	JP 05029031	B4	19930428		
PRAI	JP 1985-124617		19850607		
OS	CASREACT 106:213946				
GI					



I

AB The title compds. (I; X = halo, alkyl, alkoxy; R = H, alkyl; when X = alkyl, R = alkyl) and their pharmaceutically acceptable salts and/or hydrates, inhibiting blood platelet aggregation and biosynthesis of thromboxane A2, thereby useful for prophylaxis and treatment of asthma, heart ailments, high blood pressure, nephritis, etc. (no data), were prepd. Thus, a mixt. of 4-(.alpha.-hydroxy-2-chloro-5-iodobenzyl)-3,5-dimethylbenzoic acid, imidazole, K2CO3, KF and Cu powder in DMF was heated at 135-140.degree. for 30 h to give I (X = Cl, R = H).

L4 ANSWER 39 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1987:207671 CAPLUS

DN 106:207671

TI .alpha.-(2,4,6-Trimethylphenyl)-2-methyl-5-(1-imidazolyl)benzenemethanol or its pharmaceutically acceptable salt as therapeutic agent for nephritis

IN Suzuki, Yoshio

PA Yoshitomi Pharmaceutical Industries, Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DT Patent

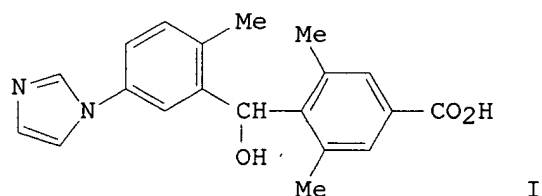
LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62010014	A2	19870119	JP 1985-147210	19850704
PRAI	JP 1985-147210		19850704		
AB	.alpha.-(2,4,6-Trimethylphenyl)-2-methyl-5-(1-imidazolyl)benzenemethanol (I) or its pharmacol. acceptable salts are effective in treating nephritis. Male Sprague-Dawley rats were treated i.v. with anti-glomerular basement membrane antiserum, followed by injection of rabbit .gamma.-globulin in complete Freund's adjuvant into the footpad to induce nephritis. I (0.3 or 3.0 mg/kg, orally) was administered to the rats from the 2nd day of i.v. antiserum injection, and the kidney was isolated on day 41 for microscopic examn. Pathol. changes were markedly reduced compared to control animals.				

L4 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1987:138446 CAPLUS
 DN 106:138446
 TI 4-[.alpha.-Hydroxy-2-methyl-5-(imidazol-1-yl)benzyl]-3,5-dimethylbenzoic acid
 IN Tsuruta, Mineo; Oe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi; Yasuda, Hiroshi
 PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 7 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 2

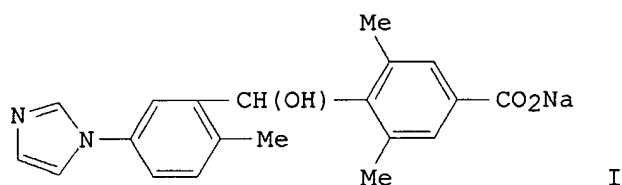
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 61277670	A2	19861208	JP 1985-121220	19850603
	JP 05041143	B4	19930622		
	US 4661603	A	19870428	US 1986-823633	19860129
PRAI	JP 1982-34365		19820303		
	US 1983-556231		19831031		
	JP 1985-121220		19850603		
OS	CASREACT 106:138446				
GI					



AB The title compd. (I), useful as cardiovascular agents, for treatment of asthma, nephritis, and for prevention of cancer metastasis, were prepd. Thus, a mixt. of 4-(2-methyl-5-iodobenzoyl)-3,5-dimethylbenzoic acid and imidazole in DMF contg. K₂CO₃, KF, and Cu powder was heated at 135.degree. for 24 h to give, after treatment with Na₂S.cntdot.3H₂O and acidification, 4-[2-methyl-5-(imidazol-1-yl)benzoyl]-3,5-dimethylbenzoic acid whose redn. with NaBH₄ in aq. NaOH at 70-75.degree. for 3 h gave, after acidification, I. This at 2.3 .times. 10⁻⁸ and >10⁻⁴ M in vitro inhibited by 50% thromboxane synthetase in human blood platelet microsomes and

cyclooxygenase in bovine seminal vesicle microsomes resp.

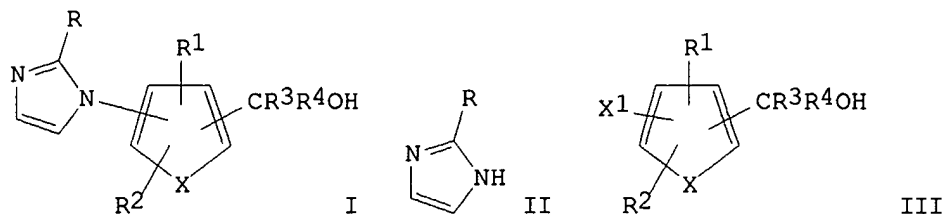
L4 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1986:545895 CAPLUS
 DN 105:145895
 TI Effects of Y-20811, a long-lasting thromboxane synthetase inhibitor, on
 thromboxane production and platelet function
 AU Mikashima, Hiroshi; Ochi, Hiroshi; Muramoto, Yoshito; Yasuda, Hiroshi;
 Tsuruta, Mineo; Maruyama, Yutaka
 CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Fukuoka, 871, Japan
 SO Thrombosis Research (1986), 43(4), 455-68
 CODEN: THBRAA; ISSN: 0049-3848
 DT Journal
 LA English
 GI



AB Effects of a new imidazole deriv., Y-20811 (I) [104363-98-6],
 on thromboxane (TX) prodn. and platelet aggregation were investigated.
 Y-20811 inhibited TX synthetase [61276-89-9] and platelet aggregation
 induced by arachidonic acid (AA) in human, guinea pig and rabbit platelets
 in vitro. Administered orally to rabbits, Y-20811 at 1 mg/kg decreased
 serum TXB2 concomitant with increasing 6-keto PGF1.alpha. and at 3 mg/kg
 inhibited AA-induced platelet aggregation, in both cases for at least 48
 h. Y-20811 (0.3 mg/kg/day) administered to rabbits for 7 days decreased
 serum TXB2 levels by 50-90% during the medication, and these levels were
 restored to initial values 3 days after withdrawal of the drug. At 1
 mg/kg, Y-20811 protected rabbits against death induced by AA (2 mg/kg).
 These results indicate that Y-20811 is a selective and long-lasting TX
 synthetase inhibitor and an antiaggregation agent useful in preventing
 thrombotic disorders.

L4 ANSWER 42 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1986:109631 CAPLUS
 DN 104:109631
 TI Imidazole derivatives
 IN Tsuruta, Mineo; Oe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi;
 Yasuda, Hiroshi
 PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 8 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

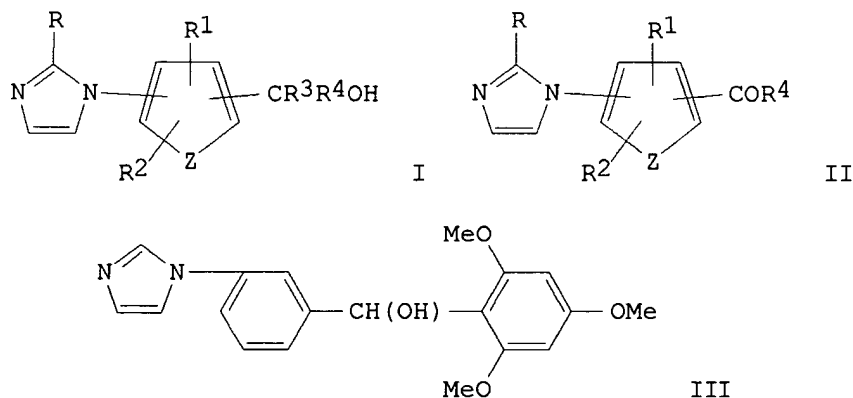
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 60142965	A2	19850729	JP 1983-163951	19830905
	JP 04015781	B4	19920319		
PRAI	JP 1983-163951		19830905		
OS	CASREACT 104:109631				
GI					



AB Title compds. I [R, R3 = H, lower alkyl; R1, R2 = H, halo, OH, lower alkyl, lower alkoxy, aralkyloxy, NO2, NH2; X = O, S, CH:CH, CH:N; R4 = (substituted) aryl] and their acid salts, useful as thromboxane A2 synthesis inhibitors, platelet aggregation inhibitors, and vasodilators, (no data), were prepd. by treating imidazoles II with alcs. III (X1 = halo). Thus, refluxing 2 g imidazole II (R = H) with 10.7 g 2,5-ClIC6H3CH(OH)C6H2Me3-2,4,6 in DMF contg. 4.3 g K2CO3, 0.3 g Cu, and 0.3 g KF for 4.5 h gave 7.7 g 2,5-ClQC6H3CH(OH)C6H2Me3-2,4,6 (Q = 1H-imidazol-1-yl).

L4 ANSWER 43 OF 58 CAPLUS COPYRIGHT 2003 ACS
 AN 1985:615282 CAPLUS
 DN 103:215282
 TI Imidazole derivatives
 PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
 SO Jpn. Kokai Tokkyo Koho, 13 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 60034952	A2	19850222	JP 1983-53333	19830328
PRAI	JP 1983-53333		19830328		
OS	CASREACT 103:215282				
GI					



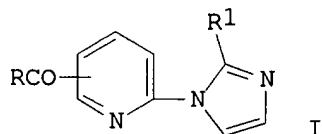
AB Sixty-three imidazole alc. derivs. I [R, R3 = H, alkyl; R1, R2 = H, halo,

09/979,509

OH, alkyl, etc.; Z = O, S, CH:CH, CH:N; R4 = aryl, (un)substituted thienyl, pyridyl, furyl] were prepd., e.g., by redn. of ketones II. Blood platelet aggregation inhibitory data of I were shown using rabbit plasma (68-100 % inhibition at 10 mg/kg orally in rats) with LD50 >1000 mg/kg. Thus, 3.4 g NaHB4 in H2O was added to 16 g 3-(1-imidazolyl)-2',4',6'-trimethylbenzophenone in EtOH and the mixt. stirred 20 h at 56.degree. to give 13.6 g .alpha.-(2,4,6-trimethylphenyl)-3-(1-imidazolyl)benzenemethanol.

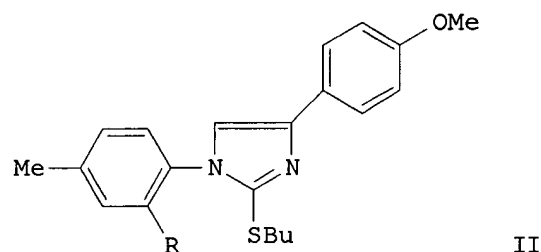
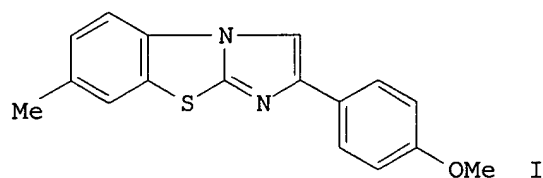
L4 ANSWER 44 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1985:62232 CAPLUS
DN 102:62232
TI 2-(1-Imidazolyl)-3(or 5)-aroylpyridines
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 59139379	A2	19840810	JP 1983-13201	19830129
	JP 01007074	B4	19890207		
PRAI	JP 1983-13201		19830129		
GI					



AB Twenty-nine title pyridines (I) (R = Ph, 4-chlorophenyl, 5-methyl-2-hydroxyphenyl, 2-methyl-3-indolyl, 6-methoxy-2-naphthyl, etc.; R1 = H, Me, Et2NCH2), having analgesic, antiinflammatory, and other activities (no data), were prepd. Thus, 29.6 g imidazole were stirred with NaH in DMF 1 h, then treated with 50 g 2-chloro-3-cyanopyridine to give 50 g 2-(1-imidazolyl)-3-cyanopyridine, which (20 g) was stirred with PhMgBr in Et2O-C6H6 and hydrolyzed to give 16.7 g I (R = 3-Ph, R1 = H).

L4 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1984:472665 CAPLUS
DN 101:72665
TI Imidazo[2,1-b]benzothiazole. Nucleophilic substitution reaction on sulfur by n-butyllithium
AU Mase, Toshiyasu; Murase, Kiyoshi
CS Cent. Res. Lab., Yamanouchi Pharm. Co., Ltd., Tokyo, 174, Japan
SO Heterocycles (1984), 22(5), 1013-15
CODEN: HTCYAM; ISSN: 0385-5414
DT Journal
LA English
OS CASREACT 101:72665
GI



AB Imidazobenzothiazole deriv. I was converted to 1-phenyl-2-(butylthio)imidazoles II [R = CO₂H, H, 4-MeC₆H₄CH(OH)]. I was treated with BuLi in THF, and the organolithium intermediate was quenched with 4-MeC₆H₄CHO to give II [R = 4-MeC₆H₄CH(OH)].

L4 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2003 ACS

AN 1984:103343 CAPLUS

DN 100:103343

TI Imidazole derivatives

IN Tsuruda, Mineo; Oe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi; Yasuda, Hiroshi

PA Yoshitomi Pharmaceutical Industries, Ltd., Japan

SO PCT Int. Appl., 37 pp.

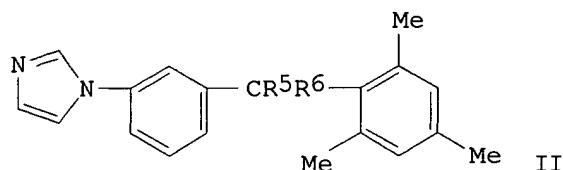
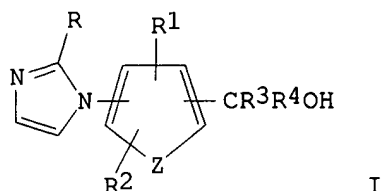
CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8303096	A1	19830915	WO 1983-JP60	19830228
	W: US				
	RW: AT, BE, DE, FR, GB, NL, SE				
	JP 58150566	A2	19830907	JP 1982-34365	19820303
	JP 03016348	B4	19910305		
	EP 110996	A1	19840620	EP 1983-900734	19830228
	EP 110996	B1	19860903		
	R: AT, BE, DE, FR, GB, NL, SE				
	AT 21895	E	19860915	AT 1983-900734	19830228
	CA 1244032	A1	19881101	CA 1983-435834	19830831
	US 4581369	A	19860408	US 1983-556231	19831031
PRAI	JP 1982-34365		19820303		
	EP 1983-900734		19830228		
	WO 1983-JP60		19830228		
OS	CASREACT 100:103343				
GI					



AB Seventy imidazole derivs. I (R, R3 = H, alkyl; R1, R2 = H, halo, alkyl, HO, alkoxy, aryloxy, O2N, H2N; R4 = aryl, thienyl, pyridyl, furyl; Z = O, S, CH:CH, CH:N), effective blood platelet aggregation inhibitors at 10 mg/kg and cyclooxygenase inhibitors at 2.3 .times. 10⁻⁶ to 1.8 .times. 10⁻⁷ mol, were prepd. Thus, 3.4 g NaBH₄ in H₂O was added to a suspension of 16 g benzophenone II (R5R6 = O) in EtOH and stirred 20 h at 56.degree. to give 13.6 g alc. deriv. (II; R5 = H, R6 = HO).

L4 ANSWER 47 OF 58 USPATFULL

AN 2003:72018 USPATFULL

TI Thromboxane inhibitors, compositions and methods of use

IN Tejada, Inigo Saenz de, Madrid, SPAIN

PI US 2003050305 A1 20030313

AI US 2002-285620 A1 20021101 (10)

RLI Continuation of Ser. No. WO 2001-US16318, filed on 22 May 2001, PENDING

PRAI US 2000-205536P 20000522 (60)

DT Utility

FS APPLICATION

LREP EDWARD D GRIEFF, HALE & DORR LLP, 1455 PENNSYLVANIA AVE, NW, WASHINGTON, DC, 20004

CLMN Number of Claims: 73

ECL Exemplary Claim: 1

DRWN 8 Drawing Page(s)

LN.CNT 2750

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention describes methods for treating or preventing sexual dysfunctions in males and females, and for enhancing sexual responses in males and females by administering a therapeutically effective amount of at least one thromboxane inhibitor, and, optionally, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase, and/or at least one vasoactive agent. The male or female may preferably be diabetic. The present invention also provides novel compositions comprising at least one thromboxane inhibitor, and, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase, and, optionally, at least one therapeutic agent, such as, vasoactive agents, nonsteroidal antiinflammatory compounds (NSAIDs), selective cyclooxygenase-2 (COX-2) inhibitors, anticoagulants, angiotensin converting enzymes (ACE) inhibitors, angiotensin II receptor antagonists, renin inhibitors, and mixtures thereof. The present

invention also provides methods for treating or preventing ischemic heart disorders, myocardial infarction, angina pectoris, stroke, migraine, cerebral hemorrhage, cardiac fatalities, transient ischaemic attacks, complications following organ transplants, coronary artery bypasses, angioplasty, endarterectomy, atherosclerosis, pulmonary embolism, bronchial asthma, bronchitis, pneumonia, circulatory shock of various organs, nephritis, graft rejection, cancerous metastases, pregnancy-induced hypertension, preeclampsia, eclampsia, thrombotic and thromboembolic disorders, intrauterine growth, gastrointestinal disorders, renal diseases and disorders, disorders resulting from elevated uric acid levels and dysmenorrhea, and for inhibiting platelet aggregation or platelet adhesion or relaxing smooth muscles.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 48 OF 58 USPATFULL
 AN 2002:301648 USPATFULL
 TI Method for prophylaxis and treatment of diabetic complications with 4[alpha-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid and derivatives
 IN Hayashi, Yoshiharu, Iruma-shi, JAPAN
 Goto, Nobuharu, Iruma-shi, JAPAN
 PI US 2002169194 A1 20021114
 AI US 2002-80660 A1 20020225 (10)
 RLI Continuation of Ser. No. US 2001-850000, filed on 8 May 2001, ABANDONED
 Division of Ser. No. US 2000-498481, filed on 4 Feb 2000, PATENTED
 Division of Ser. No. US 1998-91993, filed on 26 Jun 1998, PATENTED A 371 of International Ser. No. WO 1996-JP3776, filed on 24 Dec 1996, UNKNOWN
 PRAI JP 1995-340161 19951227
 DT Utility
 FS APPLICATION
 LREP WENDEROTH, LIND & PONACK, L.L.P., 2033 K STREET N. W., SUITE 800, WASHINGTON, DC, 20006-1021
 CLMN Number of Claims: 24
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 653

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to an agent for the prophylaxis and treatment of diabetic complications comprising, as an active ingredient, 4-[alpha-hydroxy-2-methyl-5(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof. The present invention further relates to a method for the prophylaxis and treatment of diabetic complications comprising administering an effective amount of this compound. The medicament of the present invention is useful for the prophylaxis and treatment of diabetic complications, namely, diabetic neuropathy, nephropathy, ophthalmopathy, arteriosclerosis and the like. The action of the drug is long-lasting for very small doses and a single administration a day is sufficient

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 49 OF 58 USPATFULL
 AN 2001:194442 USPATFULL
 TI Method for prophylaxis and treatment of diabetic complications with 4[alpha-hydroxy-2-methyl-5(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid and derivatives
 IN Hayashi, Yoshiharu, Iruma-shi, Japan
 Goto, Nobuharu, Iruma-shi, Japan

09/979,509

PI US 2001036957 A1 20011101
AI US 2001-850000 A1 20010508 (9)
RLI Division of Ser. No. US 2000-498481, filed on 4 Feb 2000, GRANTED, Pat. No. US 6258834 Division of Ser. No. US 1998-91993, filed on 26 Jun 1998, GRANTED, Pat. No. US 6060496 A 371 of International Ser. No. WO 1996-JP3776, filed on 24 Dec 1996, UNKNOWN
PRAI JP 1995-340161 19951227
DT Utility
FS APPLICATION
LREP WENDEROTH, LIND & PONACK, L.L.P., 2033 K STREET N. W., SUITE 800, WASHINGTON, DC, 20006-1021
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 629

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to an agent for the prophylaxis and treatment of diabetic complications comprising, as an active ingredient, 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof. The present invention further relates to a method for the prophylaxis and treatment of diabetic complications comprising administering an effective amount of this compound. The medicament of the present invention is useful for the prophylaxis and treatment of diabetic complications, namely, diabetic neuropathy, nephropathy, ophthalmopathy, arteriosclerosis and the like. The action of the drug is long-lasting for very small doses and a single administration a day is sufficient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 50 OF 58 USPATFULL
AN 2001:107916 USPATFULL
TI Method for prophylaxis and treatment of diabetic complications with 4[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid and derivatives
IN Hayashi, Yoshiharu, Iruma, Japan
Goto, Nobuharu, Iruma, Japan
PA Welfide Corporation, Osaka, Japan (non-U.S. corporation)
PI US 6258834 B1 20010710
AI US 2000-498481 20000204 (9)
RLI Division of Ser. No. US 91993, now patented, Pat. No. US 6060496
PRAI JP 1995-340161 19951227
DT Utility
FS GRANTED
EXNAM Primary Examiner: Higel, Floyd D.
LREP Wenderoth, Lind & Ponack, L.L.P.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 601

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to an agent for the prophylaxis and treatment of diabetic complications comprising, as an active ingredient, 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof. The present invention further relates to a method for the prophylaxis and treatment of diabetic complications comprising administering an effective amount of this compound. The medicament of the present invention is useful for the prophylaxis and

treatment of diabetic complications, namely, diabetic neuropathy, nephropathy, ophthalmopathy, arteriosclerosis and the like. The action of the drug is long-lasting for very small doses and a single administration a day is sufficient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 51 OF 58 USPATFULL
 AN 2000:174847 USPATFULL
 TI Production method of optically active imidazole compound, synthetic intermediate therefor and production method thereof
 IN Kawasaki, Kazuyuki, Chikujo-gun, Japan
 Kobayashi, Haruhito, Chikujo-gun, Japan
 Ehara, Syuji, Chikujo-gun, Japan
 Sato, Hideaki, Chikujo-gun, Japan
 PA Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
 PI US 6166221 20001226
 AI US 2000-511782 20000223 (9)
 RLI Division of Ser. No. US 355096
 PRAI JP 1997-10114 19970123
 DT Utility
 FS Granted
 EXNAM Primary Examiner: McKane, Joseph K.; Assistant Examiner: Wright, Sonya
 LREP Winderoth, Lind & Ponack, L.L.P.
 CLMN Number of Claims: 10
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 673

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a method for producing an optically active 4-[(.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid or a pharmaceutically acceptable salt thereof, which includes subjecting a compound of the formula (I) wherein each symbol in the formula is as defined in the specification, to optical resolution by fractional crystallization to give an optically active compound thereof and subjecting the compound to hydrolysis reaction. According to this method, a resolution method useful for industrial large-scale production of the optically active compound of 4-[(.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid, which is useful as a thromboxane synthetase inhibitor and an agent for the prophylaxis and treatment of diabetic complications, can be obtained.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 52 OF 58 USPATFULL
 AN 2000:64963 USPATFULL
 TI Process for producing optically active imidazole compounds, intermediates for synthesizing the same, and process for producing the same
 IN Kawasaki, Kazuyuki, Fukuoka, Japan
 Kobayashi, Haruhito, Fukuoka, Japan
 Ehara, Syuji, Fukuoka, Japan
 Sato, Hideaki, Fukuoka, Japan
 PA Yoshitomi Pharmaceutical Industries, Ltd., Japan (non-U.S. corporation)
 PI US 6066739 20000523
 WO 9832740 19980730
 AI US 1999-355096 19990723 (9)
 WO 1998-JP150 19980114

09/979,509

19990723 PCT 371 date
19990723 PCT 102(e) date

PRAI JP 1997-10114 19970123
DT Utility
FS Granted
EXNAM Primary Examiner: McKane, Joseph
LREP Wenderoth, Lind & Ponack, L.L.P.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 622

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a method for producing an optically active 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid or a pharmaceutically acceptable salt thereof, which includes subjecting a compound of the formula (I) ##STR1## wherein each symbol in the formula is as defined in the specification, to optical resolution by fractional crystallization to give an optically active compound thereof and subjecting the compound to hydrolysis reaction. According to this method, a resolution method useful for industrial large-scale production of the optically active compound of 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid, which is useful as a thromboxane synthetase inhibitor and an agent for the prophylaxis and treatment of diabetic complications, can be obtained.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 53 OF 58 USPATFULL
AN 2000:57790 USPATFULL
TI Prophylaxis and treatment of diabetic complications with
4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl) benzyl]-3,5-dimethylbenzoic acid
IN Hayashi, Yoshiharu, Iruma, Japan
Goto, Nobuharu, Iruma, Japan
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan (non-U.S. corporation)
PI US 6060496 20000509
WO 9724333 19970710
AI US 1998-91993 19980626 (9)
WO 1996-JP3776 19961224
19980626 PCT 371 date
19980626 PCT 102(e) date

PRAI JP 1995-340161 19951227
DT Utility
FS Granted
EXNAM Primary Examiner: Higel, Floyd D.
LREP Wenderoth, Lind & Ponack, L.L.P.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 603

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to an agent for the prophylaxis and treatment of diabetic complications comprising, as an active ingredient, 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl) benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof. The present invention further relates to a method for the prophylaxis and treatment of diabetic complications comprising administering an effective amount of this compound. The medicament of the present invention is useful for the prophylaxis and

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treatment of diabetic complications, namely, diabetic neuropathy, nephropathy, ophthalmopathy, arteriosclerosis and the like. The action of the drug is long-lasting for very small doses and a single administration a day is sufficient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 54 OF 58 USPATFULL
AN 92:14818 USPATFULL
TI Pharmaceutical composition with improved dissolution property
IN Oda, Minoru, Nakatsu, Japan
Kino, Shigemi, Chikujo, Japan
Ogawa, Kenji, Chikujo, Japan
Shiotsuki, Takako, Chikujo, Japan
PA Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5091191 19920225
WO 8906959 19890810
AI US 1989-415356 19890925 (7)
WO 1989-JP100 19890131
19890925 PCT 371 date
19890925 PCT 102(e) date
PRAI JP 1988-23250 19880203
DT Utility
FS Granted
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Webman, E. J.
LREP Wenderoth, Lind & Ponack
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 297

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical composition of the active agent sodium 4- $[\alpha$ -hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate (a thromboxane synthetase inhibitor for treatment of diseases such as thrombosis and asthma) or its optical isomer or its hydrate with an improved dissolution property, which comprises D-mannitol and/or sodium hydrogencarbonate and at least one water-soluble polymer.

The pharmaceutical composition is such that the dissolution of the above-mentioned active agent is free from pH dependency in the digestive tract including the stomach.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 55 OF 58 USPATFULL
AN 90:38442 USPATFULL
TI Therapeutic agents
IN Smithers, Michael J., Macclesfield, United Kingdom
PA Imperial Chemical Industries PLC, London, United Kingdom (non-U.S. corporation)
PI US 4925869 19900515
AI US 1987-118227 19871103 (7)
PRAI GB 1986-26296 19861104
DT Utility
FS Granted
EXNAM Primary Examiner: Burgess Yarbrough, Amelia
LREP Cushman, Darby & Cushman
CLMN Number of Claims: 14
ECL Exemplary Claim: 1

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DRWN No Drawings

LN.CNT 1260

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns novel therapeutic agents containing a (Z)-(2-alkoxyalkyl- or 2-aryloxyalkyl-4-phenyl-1,3-dioxan-5-yl)alkenoic acid, or a related tetrazole derivative, which antagonizes one or more of the actions of thromboxane A.sub.2, together with a compound which inhibits the synthesis of thromboxane A.sub.2. The compositions are useful as medicines in treating a variety of diseases or medical conditions in which thromboxane A.sub.2 and/or other prostanoid contractile substances are involved.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 56 OF 58 USPATFULL
AN 90:19583 USPATFULL
TI Pharmaceutical compositions
IN Brewster, Andrew G., Macclesfield, United Kingdom
Brown, George R., Wilmslow, United Kingdom
Smithers, Michael J., Macclesfield, United Kingdom
PA Imperial Chemical Industries plc, London, England (non-U.S. corporation)
PI US 4908380 19900313
AI US 1987-118226 19871103 (7)
PRAI GB 1986-26297 19861104
DT Utility
FS Granted
EXNAM Primary Examiner: Yarbrough, Amelia Burgess
LREP Cushman, Darby & Cushman
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1314

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention concerns novel pharmaceutical compositions containing a 4(Z)-6-(2,4-diphenyl-1,3-dioxan-5-yl)-alkenoic acid which antagonizes one or more of the actions of thromboxane A.sub.2, together with a compound which inhibits the synthesis of thromboxane A.sub.2. The compositions are useful as medicines in treating a variety of diseases or medical conditions in which thromboxane A.sub.2 and/or other prostanoid contractile substances are involved.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 57 OF 58 USPATFULL
AN 87:30374 USPATFULL
TI Imidazole derivatives
IN Tsuruda, Mineo, Fukuoka, Japan
Oe, Takanori, Nakatsu, Japan
Kawasaki, Kazuyuki, Buzen, Japan
Mikashima, Hiroshi, Fukuoka, Japan
Yasuda, Hiroshi, Nakatsu, Japan
PA Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 4661603 19870428
AI US 1986-823633 19860129 (6)
RLI Continuation-in-part of Ser. No. US 1983-556231, filed on 31 Oct 1983, now patented, Pat. No. US 4581369, issued on 8 Apr 1986
PRAI JP 1982-34365 19820303
JP 1985-121220 19850603
DT Utility

09/979,509

FS Granted
EXNAM Primary Examiner: Brust, Joseph Paul
LREP Wenderoth, Lind & Ponack
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 739

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB .alpha.-(2,6-dimethyl-4-carboxyphenyl)-2-methyl-5-(1-imidazolyl)-benzenemethanol, pharmaceutically acceptable metal salts forms thereof, acid addition salt forms thereof, amino acid addition salt forms thereof, hydrate forms thereof and mixtures thereof.

Such compounds have inhibitory activities on biosynthesis of thromboxane A.sub.2, inhibitory activities on platelet aggregation, vasodilative activities and protective effects against liver disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 58 OF 58 USPATFULL
AN 86:20284 USPATFULL
TI Imidazole derivatives
IN Tsuruda, Mineo, Fukuoka, Japan
 Oe, Takanori, Nakatsu, Japan
 Kawasaki, Kazuyuki, Buzen, Japan
 Mikashima, Hiroshi, Fukuoka, Japan
 Yasuda, Hiroshi, Nakatsu, Japan
PA Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 4581369 19860408
 WO 8303096 19830915
AI US 1983-556231 19831031 (6)
 WO 1983-JP60 19830228
 19831031 PCT 371 date
 19831031 PCT 102(e) date
PRAI JP 1982-34365 19820303
DT Utility
FS Granted
EXNAM Primary Examiner: Brust, Joseph Paul
LREP Wenderoth, Lind & Ponack
CLMN Number of Claims: 11
ECL Exemplary Claim: 1,11
DRWN No Drawings
LN.CNT 628

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An imidazole derivative of the formula: ##STR1## wherein each of R.sup.1 and R.sup.4 is a hydrogen atom or a lower alkyl group; each of R.sup.2 and R.sup.3 is a hydrogen atom, a halogen atom, a hydroxyl group, a lower alkyl group, a lower alkoxy group, an aralkyloxy group, a nitro group or an amino group; A is --O--, --S--, --CH.dbd.CH-- or --CH.dbd.N--; Z is an aryl group, a thienyl group, a pyridyl group or a furyl group, in which definition these aromatic (heterocyclic) rings may have 1 to 3 substituents, each substituent being independently selected from a halogen atom, a lower alkyl group, a cyclic alkyl group, a lower alkoxy group, a hydroxyl group, a carboxyl group, a lower alkoxycarbonyl group, a carboxy-lower-alkoxy group, a di-lower-alkylamino-lower-alkoxy group and a nitro group; and a pharmaceutically acceptable acid addition salt thereof, a method for preparing the same and a pharmaceutical composition containing such compound. Such compounds have inhibitory activities on biosynthesis of thromboxane A.sub.2, inhibitory activities

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on platelet aggregation, vasodilative activities and protective effects
on liver disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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